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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,377	01/23/2004	Yat Sun Or	ENP-074 (4014.1074 US)	7571

38473 7590 06/02/2006

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EXAMINER	
KRISHNAN, GANAPATHY	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 06/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/763,377	OR, YAT SUN	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,14 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 14-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 12/1.6/06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 3/20/2006 has been received, entered and carefully considered. The following information provided in the amendment affects the instant application:

1. Claim 13 has been canceled.

2. New Claims 14-15 have been added.

3. Claims 1 and 6-12 have been amended.

4. Remarks drawn to claim objections rejections under 35 USC 112 second paragraph, double patenting, 102 and 103.

Claims 1-12 and 14-15 are pending in the case.

The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

Claim Objections

The objection to claim 8 has been overcome by amendment.

Double Patenting

Claims 1-2, 4-6, 10, 12 and 13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 12 and 13 of copending Application No. 10/946339 ('339 application); Claims 1-2, 4-6, 8-10 and 13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 8 of copending Application No. 10/840949 ('949 application); Claims 1-6, 8-10 and 12 are provisionally rejected under the judicially created

doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of copending Application No. 10/758409 ('409 application); Claims 1-6 and 8-13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11, 15, 17-21 and 23-28 of copending Application No. 10/436622 ('622 application); Claims 1-6 and 8-13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 and 37-40 of copending Application No. 11/008581 ('581 application); Claim 13 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,878,691 ('691 patent); Claims 1-6, 8-11 and 13 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 and 10 of U.S. Patent No. 6,645,941 ('941 patent) and Claim 13 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,764,998 ('998 patent) have been overcome by cancellation of instant claim 13 and filing a Terminal Disclaimers, which have been approved. The rejection of instant claims in view of patents '715, '620, '435, '133, '171 and '683 have been rendered moot in view of the amendment to instant claim 1.

Claim Rejections - 35 USC § 112

The rejection of claims 7-12 for lack of antecedent basis has been overcome by amendment.

The following rejections are made of record.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the process as instantly claimed using macrolide antibiotic, does not reasonably provide enablement for a process using any macrocyclic compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

(A) The breadth of the claims
(B) The state of the prior art
(C) The level of one of ordinary skill
(D) The level of predictability in the art
(E) The amount of direction provided by the inventor
(F) The existence of working examples
(G) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

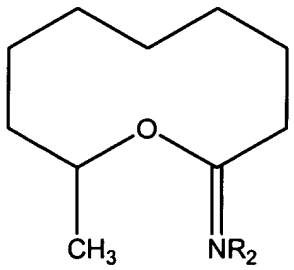
The breadth of the claims

Claim 1 is drawn to a process for making a bridged macrocyclic product comprising reacting a macrocyclic compound having at least two nucleophilic moieties with a bifunctional bridging component characterized by its ability to form a π-allyl metal complex. Claim s 14 and 15 are drawn to the same process using palladium as a

catalyst and a catalyst. The term macrocyclic compound and catalyst are broad and are seen to encompass several macrocyclic compounds other than macrolides recited in instant claim 5 and any other catalyst.

The state of the prior art

The examiner notes that the art cited by the applicants and the prior art of record, teach macrocyclic compounds mainly from the erythromycin class of macrocyclics that have several nucleophilic groups like hydroxyl, epoxy amino, etc., that can form a bridge with a bridging component. There are no examples of bridging being performed with compounds like



Both the oxygen and the nitrogen in the above structure with their electron pairs are seen as nucleophilic moieties. With no other leaving groups this macrocyclic compound that has at least two nucleophilic moieties cannot for a bridge with a bridging component as instantly claimed.

The level of predictability in the art

There is not seen sufficient data to substantiate that a bridged product as instantly claimed can be made with any macrocyclic compound comprising two nucleophilic moieties.

The amount of direction provided by the inventor

The instant specification is not seen to provide enough guidance that would allow a skilled artisan to extrapolate from the disclosure and the examples provided to enable the formation of a bridged product as instantly claimed using any macrocyclic compound comprising two nucleophilic moieties.

The existence of working examples

The working examples set forth in the instant specification are drawn to formation of a bridged product using erythromycin as the macrocyclic compound. Despite these examples there is little enabling disclosure for the same process to be extended to any macrocyclic compound.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable the use of any macrocyclic compound in the process as instantly claimed. One of ordinary skill in the art would have to carry out the process in order to determine the type of macrocyclic compound and the type of nucleophilic moiety and the type of catalyst needed to carry out the said process.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites the term derivative. In the absence of the specific derivatizations to the chemical core claimed or distinct language to describe the structural modifications or the chemical names of derivatized of this invention, the identity of the said derivatives would be difficult to describe and the metes and bounds of said derivatives applicants regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in this and any other claim in which the said term is recited.

Claim 5 recites various substituted R groups. In the absence of the specific moieties intended to effectuate modification by "substitution" or attachment to the chemical core claimed, the term "substituted" renders the claims in which it appears indefinite in all occurrences wherein applicant fails to articulate by chemical name, structural formula or sufficiently distinct functional language, the particular moieties applicant regards as those which will facilitate substitution, requisite to identifying the composition of matter claimed.

Claims that depend from a rejected base claim that is unclear/indefinite are also rendered unclear/indefinite and are rejected for the same reasons.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Or et al (WO 99/21864).

Or teaches a process wherein a macrocyclic compound having at least two nucleophilic groups (page 36, structures 10a and b) is treated with a bifunctional bridging component NH_2-(CH_2)-A-B-D-X^1 in the presence of a palladium as catalyst (page 47, lines 4-14) to get a bridged macrocyclic product 14a and b (page 36). This teaching of Or is seen to meet the limitations of instant claims 14-15.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Or et al (WO 99/21864)

Independent claim 1 is drawn to a process for the preparation of a bridged macrocyclic product comprising reacting a macrocyclic compound having at least two nucleophilic moieties

with a bridging component optionally in the presence of a catalyst. Dependent claims 3-5, 7-8 and 10-12 are drawn to various substitutions.

Or et al teaches a process for making a bridged macrocyclic compound (formula 14, page 36) comprising the reaction of the macrocyclic compound of formula 1 (page 34, has at least two nucleophilic groups) with the bridging components H_2N-$(CH_2)_m$-A-B-D-X and $(CH_2)_2$-C=CH_2 (the second bridging component with the double bond forms a pi-allyl complex with a metal; page 36, scheme 3) to yield the bridged product. The macrocyclic compound of Or is a derivative of erythromycin and is an antibiotic. The macrocyclic compound of Or is a derivative of erythromycin and is an antibiotic. The macrocyclic compound of Or (formula 1, page 34) has two sugar units attached to it. The macrocyclic compound of Or has an ethyl group attached to the carbon adjacent to the ring oxygen. This is the group L in structure I in instant claim 6. It also has a second carbonyl group (at the top left of formula 1, page 34), which corresponds to X and Y in instant claim 5 taken together to form a carbonyl group.

However, Or et al teach the use of two separate bridging components to form the bridged product instead of a single bifunctional bridging component as instantly claimed. But the two individual bridging components have a functional group on one end through which the attachment to the macrocyclic compound is achieved. One of them also has a double bond, which can form a pi-allyl metal complex.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the process of Or to make a bridged macrocyclic product as instantly claimed using a single bifunctional bridging component as instantly claimed since the starting material,

the bridging components similar to one instantly claimed and the process steps as instantly claimed is seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to use the process of the prior art for making a bridged macrocyclic compound using a single bifunctional bridging component since the use of a single bridging bifunctional component would achieve the said bridging in two steps compared to three steps that the process of Or requires. One of ordinary skill in the art would be motivated to extend this to other macrocyclic compounds in order to develop new derivatives having improved antibacterial activity since there is a continuing need to identify new derivatives which may have less potential for developing resistance (Or, page 1, lines 15-20). One of ordinary skill in the art would also recognize that the process of making the bridged macrocyclic compound could be extended with a reasonable expectation of success to other derivatives of erythromycins since all of them have the same core structure and the required nucleophilic moieties.

Conclusion

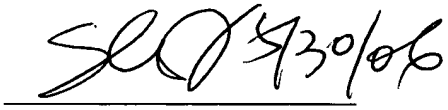
Claims 1-12 and 14-15 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GK



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